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10/773,588	02/05/2004	Louis S. Chupak	PC 25656A	6734

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EXAMINER	
ROBINSON, BINTA M	
ART UNIT	**PAPER NUMBER**
1625	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/773,588	CHUPAK ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-55 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-55 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 12/7/04;9/10/04;5/7/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The examiner notes the applicant's Election of Group II, drawn to claims 4, 15-22, 26-32, 36-42, 46-55 and parts of claims 1-3, 5-14, 23-25, 33-35, 43-45, drawn to oxaolidin-2-ones, compounds of the formulas I-V, with D = CH, E= N, and F = CH2.

Claims 2, 3, 4, 5 are objected to because they do not have a period at the end of the claims. Claims 13-15, 17, 18, 19, 21, 22, 23-31, 34-38, 41, 44-46, 48 are objected to because the period is at the end of line 1 of the claims, rather than at the end of the entire claims. Claim 16 is objected to because there is a period at the end of line 1, and the phrase "formula IID".

A further election of species has been required below:

Claims 1-54, 56-57 are generic to the following disclosed patentably distinct species: containing P, E, F, D, A, B, X, Y, Z, J, K, Q, R1 through R5 and n. The species are independent or distinct because alternative species of the genus do not anticipate one another and do not share the same properties. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument

that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

During a telephone conversation with Attorney Baude on 12/6/06 a provisional election was made with traverse to elect the species of example 4, on page 79, the confirmation of this election must be made by applicant in replying to this Office action.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 53-57 have been renumbered as claims 51-56 respectively.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-12, 38-42, 47, 50 and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 47, line 2, the radical "M" is unclear and indefinite because it is not clear if "M" is "methyl" or not.

B. Claims 50 and 53 are indefinite because they are dependent upon claim 51, which is skipped in the claims.

C. In claims 6-12, the radical "J_a" is indefinite because it is not defined in the independent claim 1, upon which claim 6 depends.

D. In claims 38-42, the radical "J_a" is indefinite because it is not defined in claim 33, upon which these claims depends.

E. In claims 48-52, the radical, "J_a" is indefinite because it is not defined in claim 43.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 15-22, 26-32, 36-42, 46-56 and claims 1-3, 5-14, 23-25, 33-35, 43-45 in part, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds of formula I with E equal to N, A equal to NH, B equal to –C(O)Me, X, Y, or Z equal to C(O), CHR3, CHR4, does not reasonably provide enablement for using the compounds of compound I, with radicals E, A, B, X, Y, or Z equal to the claimed moieties other than those stated above. The specification

does not enable any skilled pharmacologist or physician to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above.

a) Determining if any particular claimed compounds of formula I with E equal to other than N, A equal to other than NH, B equal to other than –C(O)Me, X, Y, or Z equal to other than C(O), CHR3, CHR4 would be active would require synthesis of the substrate and subjecting it to testing with Applicants' assay of compound activity against Gram positive and Gram Negative organisms. Considering the large number of compounds to be made this is a large quantity of experimentation. b) The direction concerning the claimed compounds is found in pages 62-63, 65-66, and 70-113, which merely states Applicants' intent to make and use such compounds. c) In the instant case none of the working examples contains any radical E equal to other than N, A equal to other than NH, B equal to other than –C(O)Me, X, Y, or Z equal to other than C(O), CHR3, CHR4. d) The nature of the invention is treating a bacterial infection, or treating or preventing an infectious disorder caused by a variety of bacterial agents in a mammal with Applicants' compounds. This involves physiological

activity. The nature of the invention requires an understanding of the ability of those compounds to inhibit bacterial growth. In view of the unpredictability of receptor binding activity and claimed divergent substituents with varied polarity, size, and polarisability, the skilled physician would indeed question the inclusion of such diverse rings, commensurate in scope with these claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

e) The six-membered benzene ring of Applicants' rejected examples compounds is non-basic. The pyridine ring, of the working example is strongly basic, for example. The pyridine ring of the working examples is a hydrogen bond acceptor. The benzene ring of Applicants' working examples is not. The pyridine ring and the pyrazine ring of the rejected compounds are π-electron deficient. The benzene ring of Applicants' working examples is not. There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (I) will all share the same biological properties. The diverse claimed rings are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally

dissimilar compounds will have such activity, *In re Surrey* 151 USPQ 724 (compounds actually tested which demonstrated the asserted psychomotor stimulatory and anti-convulsant properties were those having the 3,4-dichlorophenyl substituent at the 2-position on the thiazolidone nucleus not sufficient for enablement of any heterocyclic radical at the same position). *In re Fouche*, 169 USPQ 429 at 434 (a Markush group including both aliphatic and heterocyclic members not enabled for the use of those compounds within the claim having heterocyclic moieties.) *In re CAVALLITO AND GRAY*, 127 USPQ 202 (claims covering several hundred thousand possible compounds, of which only thirty are specifically identified in appellants' application, not enabled unless all of the thirty specific compounds disclosed had equal hypotensive potency because that fact would strongly indicate that the potency was derived solely from the basic structural formula common to all of them. A wide variation in such potency would suggest that it was due in part to the added substituents and might be eliminated or even reversed by many of the possible substituents which had not been tried.)

f) The artisan using Applicants' invention to treat diseases with the claimed compounds would be a physician with a MD degree and several

years of experience. He would be unaware of how to predict *a priori* how a changing a heterocyclic ring would affect biological activity. In view of the divergent rings with varied basicity, steric hindrance, and polarisability, the skilled physician would indeed question the inclusion of such fused rings, commensurate in scope with these claims. g) Physiological activity, is well-known to be unpredictable, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of millions of compounds of formula (I). Thus, the scope is very broad. The present claims embrace various heterocyclic radicals, which are not art-recognized as equivalent. The specific compounds made are not adequately representative of the compounds embraced by the extensive Markush groups instantly claimed.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed

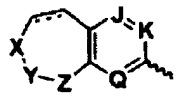
invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

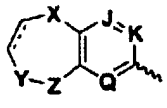
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 11-53 are rejected under 35 U.S.C. 102(e) as being anticipated by Johnson et. al. (US 2002/0133021 A1)

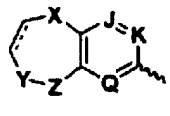
Johson et. al. anticipates the instant claims because it discloses the compounds, Example 20, example 21, example 23, example 25, example 26, example 28, example 36, example 38, example 39, example 47, example 48, example 49, example 50 and these compounds have antibacterial activity and a method of treating or combating, bacterial infections in warm-blooded animals is disclosed. At column 8, paragraph 0208, see the method of using these compounds to treat bacterial infections and at column 20, paragraph 0318, see example 20, at column 21, paragraph 0333, see example 21, at column 22, paragraph 0349, see example 23, and at paragraph 0356, column 22, see example 25, at column 23, paragraph 0358, see example 26, at column

23, paragraph 0362, see example 28, at column 25, paragraph 0378, see the example of 36, at column 26, paragraphs 0391 and 0393, see examples 38 and 39. At column 28, paragraph 0412, see example 47. At column 29, paragraph 0426, see example 48. At column 30, paragraphs 0428 and 0433, see examples 49 and 50. Example 47 at claim 28, paragraph 0412, anticipates the claims particularly, claim 55, which contains the same exact chemical compound at line 34, page 149, because the moiety analogous to the instant P is 3-benzothiepin-y-yl), the moieties analogous to the instant P is 

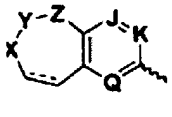
J, K, and Q is CH, and the moiety analogous to has a X group wherein X is S, and Y and Z are CH2, and the moieties analogous to E is N, the moiety analogous to F is CH2, the moiety analogous to D is CH, the moiety analogous to A is NH and the moiety analogous to B is CH3. The compound of example 20 anticipates the claims because the moiety analogous to the instant E is N, the moiety analogous to the instant F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous the instant B is CH3, the moiety analogous to the instant P when P is equal to 

, wherein the moiety analogous to the instant X is C(O)H, the moiety analogous to the instant Y and Z are CH2, the moiety analogous to the instant E is N, the moiety analogous the instant F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the

moiety analogous to the instant B is C(=O)R1, wherein the moiety analogous to the instant R1 is methyl.

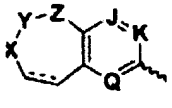
The compound of example 21 anticipates the claims because the moiety analogous to the instant E is N, the moiety analogous to the instant F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous the instant B is CH3, the moiety analogous to the instant P when P is equal to 

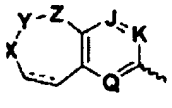
, wherein the moiety analogous to the instant X is C(O)H, the moiety analogous to the instant Y and Z are CH2, the moiety analogous to the instant E is N, the moiety analogous the instant F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(=S)R1, wherein the moiety analogous to the instant R1 is methyl.

Example 23 anticipates the claims because the moiety analogous to the instant E is N, the moiety analogous to the instant A is NH, the moiety analogous the instant B is C(O)CH3, the moiety analogous to the instant P is 

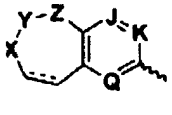
wherein the X is N(C=O)R5, wherein R5 is equal to H, and Y and Z are CH2, the moieties analogous to the instant J, K, and Q are CH, the moiety analogous to the instant D is CH, the moiety analogous to the instant F is CH2, the moiety analogous to the instant A is NH, the moiety

analogous to the instant B is C(O)R1, and the moiety analogous to the instant R1 is CH3.

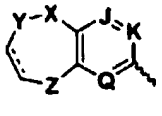
Example 25 anticipates the claims because the moiety analogous to the instant E is N, the moiety analogous to the instant A is NH, the moiety analogous the instant B is C(O)CH3, the moiety analogous to the instant P is  wherein the X is N(C=O)R5, wherein R5 is equal to CH3, and Y and Z are CH2, the moieties analogous to the instant J, K, and Q are CH, the moiety analogous the instant D is CH, the moiety analogous to the instant F is CH2, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(O)R1, and the moiety analogous to the instant R1 is CH3.

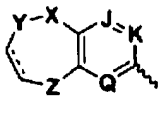
The compound of example 26 anticipates the claims because of the moiety analogous to the instant E is N, the moiety analogous to the instant A is NH, the moiety analogous the instant B is C(O)CH3, the moiety analogous to the instant P is  wherein the X is N(C=O)R5, wherein R5 is equal to -OCH3, and Y and Z are CH2, the moieties analogous to the instant J, K, and Q are CH, the moiety analogous the

instant D is CH, the moiety analogous to the instant F is CH2, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(O)R1, and the moiety analogous to the instant R1 is CH3.

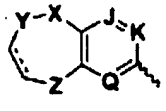
The compound of example 28 anticipates the claims because of the moiety analogous to the instant E is N, the moiety analogous to the instant A is NH, the moiety analogous the instant B is C(O)CH3, the moiety analogous to the instant P is  wherein the X is NS02R5, wherein R5 is equal to -CH3, and Y and Z are CH2, the moieties analogous to the instant J, K, and Q are CH, the moiety analogous the instant D is CH, the moiety analogous to the instant F is CH2, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(O)R1, and the moiety analogous to the instant R1 is CH3.

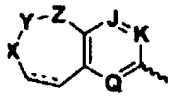
The compound of example 36 anticipates the instant claims because the moiety analogous to the instant E is N, the moiety analogous to the instant moiety F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(O)CH3, the moiety analogous to the instant P, wherein P is

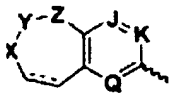
 , wherein the Y is NC(=O)R5, wherein the R5 is methyl, the moiety analogous to the instant X and Z are CH2, the moieties analogous to the instant J, K, and Q are CH, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(O)R1, wherein R1 is CH3., the moiety analogous to the instant F is CH2.

The compound of example 38 anticipates the instant claims because the moiety analogous to the instant E is N, the moiety analogous to the instant F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(=O)R1, wherein R1 is CH3, the moiety analogous to the instant P group wherein the P group is  , wherein J, K, and Q are CH, X, and Z are CH2, and Y is N(C=O)R5, wherein R5 is CH3.

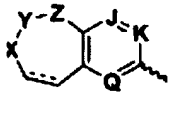
The compound of example 39 anticipates the instant claims because the moiety analogous to the instant E is N, the moiety analogous to the instant F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(=O)R1, wherein R1 is CH3, the moiety analogous to the instant P group

wherein the P group is  , wherein J, K, and Q are CH, X, and Z are CH2, and Y is N(C=O)OR5, wherein R5 is CH3.

Example 48 anticipates the claims because the moiety analogous to the instant E is N, the moiety analogous to the instant F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(O)CH3, the moiety analogous to the instant P is  wherein X is SO2, and Y and Z are CH2, the moieties analogous to the instant J, K and Q are CH.

Example 49 anticipates the claims because the moiety analogous to the instant E is N, the moiety analogous to the instant F is CH2, the moiety analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(S)R1 wherein R1 is CH3, the moiety analogous to the instant P is  wherein X is S, and Y and Z are CH2, the moieties analogous to the instant J, K and Q are CH.

Example 50 anticipates the claims because the moiety analogous to the instant E is N, the moiety analogous to the instant F is CH2, the moiety

analogous to the instant D is CH, the moiety analogous to the instant A is NH, the moiety analogous to the instant B is C(S)R1 wherein R1 is CH3, the moiety analogous to the instant P is  wherein X is SO2, and Y and Z are CH2, the moieties analogous to the instant J, K and Q are CH.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 11-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et. al. (US 2002/0133021 A1) based on the 102 e date.

Johnson et. al. teaches a compound of the formula I, wherein Y is –NHC(=W)R1, -O-het, -S-het. or –NH-het, -O-, -NR3-, -S(=O)l-, R1 is moieties a-h, wherein >G-E- is >N-C and Q is a carbon atom; aryl is a phenyl radical or an ortho-fused bicyclic carbocyclic radical wherein at least one ring is aromatic; het is a C-linked- five (5) or six (6) membered saturated or unsaturated heterocyclic ring having 1, 2 or 3 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen, which is optionally fused to a benzene ring, m is 0, 1, 2, 3, or 4; n is 0, 1, 2, 3, or 4 with the proviso that m and n taken together are 3 or 4; and l is 0, 1, or 2,

pharmaceutical compositions containing them, and a method of treating bacterial infections in a mammal with said compounds.

The difference between the prior art compound, compositions and method of treating and the instantly claimed compounds, composition and method of treating is the teaching of a genus of compounds which overlaps in subject matter with the instant genus of compounds. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds. For instance, see the compound, of example 48, where a disclosed species is exemplified. Accordingly, the compounds, compositions and method of treating are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds, compositions and method of treating over those of the generic prior art compounds, compositions and method of treating.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Thomas McKenzie can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
January 24, 2007

TAYLOR VICTOR OH
PRIMARY EXAMINER

1/29/07